EXHIBIT A

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ALCON INC., ALCON VISION, LLC, and ALCON LABORATORIES, INC., *Plaintiffs*, v. PADAGIS ISRAEL PHARMACEUTICALS LTD., PADAGIS US LLC, and PADAGIS LLC, *Defendants*.	§ § § § § § § § § § § § §	Civil Action No. 22-1422-WCB [redacted]

CLAIM CONSTRUCTION ORDER

In this Hatch-Waxman Act patent case, plaintiffs Alcon Inc., Alcon Vision, LLC, and Alcon Laboratories, Inc., (collectively, "Alcon") have asserted U.S. Patent Nos. 9,044,484 ("the '484 patent") and 9,421,265 ("the '265 patent") against defendants Padagis Israel Pharmaceuticals Ltd., Padagis US LLC, and Padagis LLC (collectively, "Padagis"). The parties have raised several claim construction issues and have filed briefs outlining their positions on those issues. Dkt. Nos. 57, 64, 67, 71. On September 6, 2023, I held a claim construction hearing. This order addresses the disputes raised in the parties' briefs and at the hearing.

The '484 and '265 patents are generally directed to multi-dose ophthalmic compositions that have "sufficient antimicrobial activity to satisfy the preservation efficacy requirements of the United States Pharmacopeia ('USP') and analogous guidelines in other countries." '484 patent, col. 1, ll. 26–30. As the specification of the '484 patent explains,[1] the preservatives used in

[1] The specifications of the two asserted patents are substantially equivalent and do not differ for purposes relevant to the claim construction disputes in this case. For simplicity, the references to the specification in this order are exclusively to the '484 patent.

ophthalmic compositions may come in contact with the cornea when the composition is administered. *Id.* at col. 2, ll. 2–3. The cornea, however, is "particularly sensitive to exogenous chemical agents," and thus exposure to antimicrobial preservatives may have "harmful effects on the cornea." *Id.* at col. 2, ll. 3–6. For that reason, "[b]alancing the anti-microbial efficacy and potential toxicological effects of anti-microbial preservatives is sometimes difficult to achieve." *Id.* at col. 2, ll. 9–11.

One preservative that is often used in compositions in which other preservatives can be ineffective is benzalkonium chloride ("BAC"). *Id.* at col. 2, ll. 30–33. Below certain threshold concentration levels, BAC can "exhibit significantly lower toxicological effects" but also can "rapidly lose its anti-microbial efficacy." *Id.* at col. 2, ll. 33–38. As such, the inventors of the asserted patents sought to develop "a preservative system that can enhance the anti-microbial effects of low concentrations of BAC such that BAC can be used in situations where other preservatives might be ineffective." *Id.* at col. 2, ll. 38–42. At a high level of generality, the compositions described by the inventor of the asserted patents are "multi-dose ophthalmic composition[s]" that include a first polyol,[2] a second polyol, borate, and BAC. *Id.* at col. 3, ll. 25–27.

Claim 1 of the '484 patent is generally representative of the claims of the asserted patents. That claim recites as follows:

> 1. A multi-dose ophthalmic composition, comprising:
>
> a therapeutically effective amount of brimonidine;

[2] The asserted patents use the term "polyol" to refer to "any compound having at least one hydroxyl group on each of two adjacent carbon atoms that are not in trans configuration relative to each other." '484 patent, col. 4, ll. 5–8. Examples of the inventor's preferred polyols include "mannitol, glycerin, xylitol, sorbitol, and propylene glycol." *Id.* at col. 4, ll. 12–14.

> a first polyol, the first polyol being selected from mannitol, sorbitol or a combination thereof wherein the concentration of the first polyol in the composition is at least 0.15 w/v % but is less than 0.5 w/v %;
>
> a second polyol, the second polyol being selected from propylene glycol, glycerine or a combination thereof wherein the concentration of the second polyol in the composition is at least 0.3 w/v % but less than 1.2 w/v % of the composition;
>
> borate in the composition at a concentration that is at least 0.1 w/v % but less than about 0.5 w/v %;
>
> BAC as an anti-microbial preservative, the concentration of BAC in the composition being greater than 0.0007 w/v % but less than 0.0035 w/v %; and
>
> water;
>
> wherein the composition has a pH that is at least 4 but less than 7.0.

'484 patent, cl. 1.

A. Agreed-Upon Constructions

At the outset, I note that the parties have agreed to constructions of two terms that were originally identified as disputed in the parties' joint claim construction chart. Specifically, Padagis has agreed to adopt Alcon's proposed constructions of the following limitations: (1) In claim 15 of the '484 patent, "a second polyol, the second polyol being selected from propylene glycol, glycerine or a combination thereof wherein the concentration of the second polyol in the composition is at least about 0.3 w/v % but less than about 1.2 w/v % borate [sic] in the composition at a concentration that is at least 0.1 w/v % but less than about 0.5 w/v %"; and (2) In claims 17 and 22 of the '484 patent, the limitation "with the viscosity of the suspension being measured at a high shear rate of sec^{-1} [or sec-1] [sic] at room temperature." Dkt. No. 64 at 4 n.1. In light of the parties' agreement, I will adopt Alcon's proposed constructions of those terms, which are set forth in the parties' joint claim construction chart. *See* Dkt. No. 53 at 2–3.

B. "free of any preservatives other than [BAC]"

The first limitation disputed by the parties appears in claims 15 and 22 of the '484 patent and their dependent claims.[3] Claims 15 and 22 recite compositions similar to those recited in claim 1 of the '484 patent, but they also require that the compositions be "free of any preservatives other than [BAC]." '484 patent, claims 15, 22. The parties dispute the proper construction of that limitation.

Alcon argues that the limitation should be construed to mean that "[t]he composition is entirely devoid of any preservative agent that prevents the proliferation of microbes in an ophthalmic composition, other than BAC, as differentiated from excipients such as borate and polyols that merely enhance anti-microbial activity." Dkt. No. 57 at 4.

Padagis submits that the term "preservative" means "a chemical agent that prevents the proliferation of microbes in a composition." In view of that definition, Padagis argues that claims 15 and 22 of the '484 patent are indefinite because the claims require the presence of "borate," which Padagis characterizes as a preservative. Dkt. No. 64 at 8. Padagis argues that if borate is considered a preservative, it would be impossible for a composition to both contain borate and be "free of any preservatives other than [BAC]." *See* '484 patent, claims 15, 22.

There are two problems with Padagis's reasoning. First, the claims themselves make clear that a "preservative," as that term is used in the '484 patent, is distinct from the other elements of the claims, such as borate and polyols. Claim 22, for example, recites several distinct components of the composition: (1) brimonidine; (2) mannitol; (3) propylene glycol; (4) borate; (5)

[3] The phrase "substantially free of any preservatives other than [BAC]" appears in claim 7 of the '484 patent and in claims 7 and 13 through 20 of the '265 patent. The parties' arguments with respect to this limitation apply equally to those claims. Padagis raises additional arguments with respect to the "substantially free" limitations, which I address separately below.

carboxyvinyl polymer; (6) BAC as "an anti-microbial preservative"; and (7) water. *Id.* at claim 22. To conclude that any one of those above elements, other than BAC, is a preservative would leave the claim with no scope, because the claim also requires that the composition be "free of any preservatives other than [BAC]." *See id.* As the Federal Circuit has explained, "[a] claim construction that renders asserted claims facially nonsensical 'cannot be correct.'" *Becton, Dickinson & Co. v. Tyco Healthcare Grp., LP*, 616 F.3d 1249 (Fed. Cir. 2010) (quoting *Schoenhaus v. Genesco, Inc.*, 440 F.3d 1354, 1357 (Fed. Cir. 2006)). For that reason, the claims themselves indicate that the term "preservative," as used in the '484 patent, was not meant to include borate or polyols.[4]

Second, the specification makes it clear that the '484 patent distinguishes "preservatives" from borate and polyols. That point is made most clearly in column 1 of the patent, which explains that "the present invention relates to aqueous pharmaceutical compositions . . . containing two or more different polyols in conjunction with borate and a preservative." '484 patent, col. 1, ll. 17–21. The specification later explains that "[t]he present invention is predicated upon the provision of two or more different polyols in the presence of borate and [BAC]." *Id.* at col. 3, ll. 41–43; *see also id.* at col. 6, ll. 30–34. Furthermore, the specification expressly identifies some preservatives other than BAC that may be added to the composition:

> The composition of the present invention can include other preservatives in addition to BAC. Potential additional preservatives include, without limitation, hydrogen peroxide and polymeric quaternary ammonium compounds. However, it is

[4] That conclusion is further reinforced by the dependent claims of the '484 patent. For example, dependent claim 19 of the '484 patent adds a limitation that the composition be "free of any anti-infective or anti-biotic ophthalmic drug." The specification explains that such drugs are preservative aids; that is, they are "therapeutic agents that aid . . . preservation." '484 patent, col. 7, ll. 35–41. If claim 15, the independent claim from which claim 19 depends, were construed to require that the composition be free of preservative aids, then claim 19 would not limit claim 15 in any respect and would therefore be superfluous.

> preferable that the composition be substantially free or entirely free of any preservatives other than BAC.

Id. at col. 4, ll. 34–39.

The purpose of including borate and polyols in the claimed compositions, the specification explains, is to "enhance anti-microbial activity in the presence of a preservative such as a polymeric quaternary ammonium." *Id.* at col. 2, ll. 52–54. That is, those components are distinct from preservatives, but they "enhance anti-microbial activity" when a preservative is present. *Id.*; *see also id.* at col. 5, ll. 51–57. Those details in the specification further underscore the point that the term "preservative," as used in the asserted patents, does not include borate or polyols.

For its part, Padagis points to a passage in the specification in which the term "antimicrobial preservative" is defined to mean "a chemical agent that prevents the proliferation of microbes in a composition." Dkt. No. 64 at 5 (quoting '484 patent, col. 1, ll. 60–63). Padagis asserts that the definition of "antimicrobial preservative" in that passage clearly includes borate and polyols, and that Alcon is simply attempting to append a negative limitation to that definition. *Id.*

On its face, the definition of "antimicrobial preservative" would appear to encompass borate and polyols. However, as noted, for purposes of the asserted patents substances such as borate and polyols that merely "enhance anti-microbial activity in the presence of a preservative" are not themselves considered preservatives. '484 patent, col. 2, ll. 51–54. Moreover, the distinction between a preservative and a preservative enhancer would be well understood by a skilled artisan. In fact, Padagis's Abbreviated New Drug Application ("ANDA") submission drew an express contrast between [redacted], which the ANDA referred to as a "[p]reservative [a]gent," and [redacted], which the ANDA referred to as a "preservative aid." Dkt. No. 57-6 at 3.[5]

[5] In support of its contention that borate is considered an antimicrobial preservative, Padagis cites the American Pharmacists Association's *Handbook of Pharmaceutical Excipients* 74 (5th ed. 2006), which states that boric acid "is used as an antimicrobial preservative" in various

The term "preservatives" will therefore be construed to include substances such as BAC, hydrogen peroxide, and polymeric quaternary ammonium compounds, which prevent the proliferation of microbes in a composition. The term will not be construed to include substances such as borate or polyols, which merely enhance the anti-microbial effect of a preservative.

C. "substantially free of any preservatives other than [BAC]"

Claim 7 of the '484 patent and claims 7 and 13 through 20 of the '265 patent require that the claimed compositions be "substantially free of any preservatives other than [BAC]." In addition to the arguments made with respect to the phrase "free of any preservatives other than [BAC]," Padagis argues that this limitation is indefinite because the specification provides insufficient guidance as to whether a particular compound is "substantially free" of non-BAC preservatives. Dkt. No. 64 at 11–12. Alcon argues that a composition is "substantially free" of an ingredient if the composition is "entirely devoid of or includes only a nominal amount of that ingredient." Dkt. No. 57 at 9.

The specification explains that the phrase "substantially free of," as it refers to an ingredient of the ophthalmic composition, means that "the ophthalmic solution can be either entirely devoid of that ingredient or includes only a nominal amount of that particular ingredient." '484 patent, col. 4, ll. 40–44. That definition, Padagis argues, is insufficient because it does not specify an upper limit for what constitutes a "nominal amount." Padagis points to a passage in the

products. Dkt. No. 64-3 at 5. The other items of extrinsic evidence in the record, however, do not support Padagis's position, but instead characterize the function of borates as enhancing the effectiveness of antimicrobial preservatives, or as a "preservative aid." A paper by Olga Borokhov and David Schubert titled *Antimicrobial Properties of Boron Derivatives* (2007), cited by Padagis, states that "the presence of boric acid in antimicrobial formulations can enhance performance and significantly reduce the amount of another active ingredient." Dkt. No. 64-4 at 429. And U.S. Patent Application Publication No. 2008/0095863, Dkt. No. 67-5 ¶ 75, characterizes boric acid as a "preservative aid," distinguishing boric acid from several substances referred to as preservatives, preservation agents, or anti-microbial agents.

specification that states the following: "BAC is typically in the compositions of the present invention in an amount that is greater than about 0.00001 w/v %." '484 patent, col. 4, ll. 45–46. The implication of that passage is that 0.00001 w/v % of BAC is an amount that has an anti-microbial effect, and would not be considered nominal. Padagis argues that a skilled artisan could not readily determine whether a particular ingredient was present in a nominal amount because, in Padagis's view, "[t]he term 'nominal' loses meaning when it is contrasted with amounts as low as 0.00001%." Dkt. No. 71 at 7.

As the specification explains, one of the objectives of the claimed inventions is to "enhance the anti-microbial effects of low concentrations of BAC" so that BAC may be used "in situations where other preservatives might be ineffective." '484 patent, col. 2, ll. 39–40. Accordingly, while it may be true that a small amount of BAC (e.g., 0.00001 w/v %) would be considered more than a nominal amount of BAC, it is not necessarily the case that a similar amount of some other preservative would be considered more than a nominal amount of that other preservative. The question for a skilled artisan to answer is whether a particular ingredient is present in more than a de minimis or immaterial amount.

More generally, courts have regularly rejected contentions that claims containing terms such as "substantially" or "generally" are indefinite. *See, e.g.*, *Deere & Co. v. Bush Hog, LLC*, 703 F.3d 1349, 1359 (Fed. Cir. 2012) ("This court has repeatedly confirmed that relative terms such as 'substantially' do not render patent claims so unclear as to prevent a person of skill in the art from ascertaining the scope of the claim."); *ESCO Grp. LLC v. Deere & Co.*, No. 20-1679, 2023 WL 4199413, at *11 (D. Del. June 22, 2023) (same); *see also Otsuka Pharm. Co. v. Lupin Ltd.*, No. 21-900, 2022 WL 2952759, at *1 (D. Del. July 26, 2022) ("substantially free from" held not indefinite); *Accordant Energy, LLC v. Vexor Tech., Inc.*, No. 1:17-cv-411, 2017 WL 5588869,

at *6 (N.D. Ohio Nov. 21, 2017) ("substantially free/substantially no" held not indefinite); *Aventis Pharma Deutschland GmbH v. Lupin Ltd.*, No. 2:05-cv-421, 2006 WL 1314413, at *14 (E.D. Va. May 11, 2006) ("substantially free of other isomers" held not indefinite).

The phrase "substantially free of any preservatives other than [BAC]" is therefore not indefinite; it will be construed to refer to compositions containing no more than a de minimis or immaterial amount of preservatives other than BAC.

D. "propylene glycol wherein the concentration of the mannitol is at least 0.01 w/v % but no greater than 0.5 w/v %"

Claim 20 of the '265 patent recites a multi-dose ophthalmic composition comprising several components. As relevant to this dispute, the first limitation of claim 20 is "mannitol wherein the concentration of the mannitol is at least 0.01 w/v % but no greater than 0.5 w/v %." The second limitation of claim 20 is "propylene glycol wherein the concentration of the mannitol is at least 0.01 w/v % but no greater than 0.5 w/v %." As can be seen from the language of those limitations, the clause beginning with "wherein the concentration of the mannitol" appears in each of the first two claim limitations. Padagis argues that the duplicate limitation renders claim 20 indefinite because mannitol is not a component of propylene glycol, and thus a skilled artisan "would not understand what was intended by the 'wherein' clause following 'propylene glycol' and how it further limits the claim." Dkt. No. 64 at 13. Alcon argues that the repeated limitation should be construed according to its terms, and that the fact that language of the mannitol limitation is duplicated in the propylene glycol limitation does not render the claims indefinite.

To begin with, it is clear that the repetition of the mannitol "wherein" clause is the product of a drafting error. On its face, the "propylene glycol" limitation would appear to have no scope, as propylene glycol does not contain any concentration of mannitol. A district court may correct an "obvious error" in a patent claim where (1) "the correction is not subject to reasonable debate

based on consideration of the claim language and the specification"; and (2) "the prosecution history does not suggest a different interpretation of the claims." *CBT Flint Partners, LLC v. Return Path, Inc.*, 654 F.3d 1353, 1358 (Fed. Cir. 2011). In deciding whether a particular correction is appropriate, the court "must consider how a potential correction would impact the scope of the claim and if the inventor is entitled to the resulting claim scope based on the written description of the patent." *Pavo Sols. LLC v. Kingston Tech. Co., Inc.*, 35 F.4th 1367, 1373 (Fed. Cir. 2022) (quoting *CBT Flint*, 654 F.3d at 1359). The question is thus what was intended by the patent drafter in including the duplicated "wherein" clause in claim 20.

The problem for Alcon is that there are two possible constructions of the disputed language in the claims, and neither is likely to be correct. As to the first possibility, Alcon suggests that the second "wherein" clause relating to mannitol should be construed to refer literally to the concentration of mannitol in the claimed composition, even though that limitation is already recited once in claim 20.

That construction is nonsensical. Propylene glycol does not contain mannitol, so it makes no sense to refer to "propylene glycol wherein the concentration of mannitol" in a designated amount. Even setting aside that problem, Alcon's construction would require the presence of propylene glycol in the composition, but would provide no boundary for the concentration of propylene glycol. Given that claim 20 recites specific concentration ranges for the mannitol, borate, carboxyvinyl polymers, and BAC components of the claimed composition, it seems highly unlikely that the inventor intended for the propylene glycol component to be the only claimed component without a designated concentration range.

Another possible construction of the "wherein" clause in the propylene glycol limitation is that the duplicate reference to mannitol was intended to recite the term "propylene glycol" in place

of "mannitol," so that the full limitation would read "propylene glycol wherein the concentration of the propylene glycol is at least 0.01 w/v % but no greater than 0.5 w/v %." Such a correction would not be unreasonable on its face, because several of the independent claims of the '484 and '265 patents recite concentration ranges for propylene glycol or for the "second polyol," which encompasses propylene glycol. '484 patent, claims 1, 15, 22; '265 patent, claim 13. However, such a correction would exclude each of the examples disclosed in the specification from the scope of the claims, because it would set the upper bound for the concentration of propylene glycol at 0.5 w/v %. By contrast, all the examples disclosed in the specification that contain propylene glycol contain that polyol in a concentration of at least 0.75 w/v %. *See* '265 patent, Tables A, C, D, E, F, G, H, I. It is highly unlikely that the inventor would have sought a claim that did not cover a single preferred embodiment disclosed in the specification.

The most likely explanation for the duplicated limitation would appear to be that the patent drafter copied the "wherein" clause from the mannitol limitation and pasted it into the propylene glycol limitation without revising the clause to reflect that it was intended to refer to propylene glycol and to contain some sort of concentration range for that component. But there is no clear guidance in the intrinsic record as to what precise range of concentrations that would be.[6] For that reason, a skilled artisan would not be able to determine the scope of claim 20 "with reasonable certainty." *See Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901 (2014). Claim 20 of the '265 patent is therefore invalid for indefiniteness.

[6] One can speculate that what was intended was for the propylene glycol limitation of claim 20 to read "wherein the concentration of the propylene glycol is at least about 0.1 but less than about 5 w/v % of the composition," which is the concentration range recited in the similarly structured claim 13 of the '265 patent. But even Alcon does not argue for that construction. In any event, importing that language from claim 13 with nothing in claim 20 to support doing so would be the product of a guess, which is not a sufficient basis on which to support the construction of a disputed claim term.

E. "extend period of time of"

Claim 20 of the '484 patent and claim 18 of the '265 patent, as well as the claims that depend from those claims, require that the composition be configured for administration to the eye "repeatedly for an extend [sic] period of time of [sic] and is administered at least once a week." There are two apparent errors in that limitation. First, the word "extend" should obviously read "extended." Second, there is no specific period of time following the phrase "extend period of time of." Padagis argues that those errors render the claims indefinite. Dkt. No. 64 at 15–16. Alcon argues that the "extend period of time of" should be construed to mean "at least one month." Dkt. No. 57 at 15.

The phrase "extend period of time" appears once in the specification, in column 9, where the specification states that "the desired treatment is repeated administration of the composition . . . to the eye of the mammal for an extend period of time." '484 patent, col. 9, ll. 19–21. The specification continues by stating that the administration is "for a period of at least one month, more typically at least six months and even more typically at least one year." *Id.* at col. 9, ll. 25–29. In effect, the specification defines the nonce phrase "extend period of time" to mean a period of at least one month, but more typically at least six months and even more typically at least one year.

Given that definition of the term, it is clear that the word "of" following "extend period of time" is not necessary to a reasonable understanding of the claim. The inclusion of that word is best understood as a scrivener's error; that is, the limitation is properly read as "administered repeatedly for an extended period of time and administered at least once a week." In light of the definitional language in the specification, a skilled artisan would understand that an "extend[ed] period of time" is at least one month.

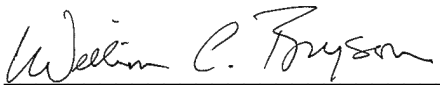
Padagis argues that the use of the word "of" following "extend period of time" indicates that the inventor had intended to claim a particular length of time—perhaps at least one month, perhaps at least six months, or perhaps at least one year. Dkt. No. 64 at 16. However, if the inventor had intended to claim a specific time period, the words "extend[ed] period of time" would be superfluous. That is, the limitation could simply have read "repeatedly for a period of at least [a specified number of] months and is administered at least once a week." Because the length of an "extend[ed] period of time" is described in the specification, *see* '484 patent, col. 9, ll. 19–29, the best reading of the claims is that the inventor intended to capture the full breadth of an "extend[ed] period of time." For that reason, the "extend[ed] period of time of" limitation is best construed to require the claimed composition to be configured for administration for a period of at least one month. Padagis has thus not met its burden of proof to show that the "extend period of time" limitation is fatally indefinite. *See Akzo Nobel Coatings, Inc. v. Dow Chem. Co.*, 811 F.3d 1334, 1343 (Fed. Cir. 2016).

* * * * *

I note that several of the parties' briefs and exhibits relating to the claim construction issues have been filed under seal. Accordingly, in an abundance of caution, this order has been filed under seal. Within three business days of the issuance of this order, the parties are directed to advise the court by letter whether they wish any portions of the order to remain under seal, and if so which portions. Any request that portions of the order should remain under seal must be supported by a particularized showing of need to limit public access to those portions of the order.

IT IS SO ORDERED.

SIGNED this 8th day of September, 2023.



WILLIAM C. BRYSON
UNITED STATES CIRCUIT JUDGE